D. Remarks

The claims are 1-8, 10-18 and 20-28, with claims 1, 16, 24, 25, 27 and 28 being independent. Claim 1 has been amended to better define the present invention. Claims 5 and 8 have been amended to reflect the changes in claim 1. New claims 24-28 have been added. Support for the amendment and the new claims may be found throughout the specification. No new matter has been added. Reconsideration of the claims is expressly requested.

Claims 1-8, 10-18 and 20-23 stands rejected under 35 U.S.C. § 102(e) as being allegedly anticipated by U.S. Patent No. 6,306,643 (Gentalen). The grounds of rejection are respectfully traversed.

Prior to addressing the merits of rejection, Applicants would like to briefly review some of the key features and advantages of the presently claimed invention. In the present invention: (i) the probe spots are arranged on a substrate divided into plural groups; (ii) hybridization signal is not measured for each probe spot (cell) but integral intensity is determined for each group; and (iii) the obtained pattern of signal intensities is used to determine the presence or absence of a certain acid (gene) in a sample. Thus, the present invention provides a method and an array substrate suitable for mass screening, allowing to rapidly determine only the presence or absence of a gene variant, without the need for an expensive apparatus and complex analysis.

Gentalen is directed to an array and a method for detecting linkage of polymorphic sites on a nucleic acid. This reference teaches that a target nucleic acid having segments complimentary to both first and second probes shows stronger normalized

binding to the region containing both probes ("pooled region") than the aggregate normalized binding that it shows for both regions each of which contains only one type of probe. Gentalen teaches that this occurs because of cooperative binding between the two probes when they bind to linked polymorphic sites on the target sequence.

Gentalen discloses a DNA chip having at least three regions (cells), one containing a pool (mixture) of two kinds of probes, with the other two regions each containing only one of these two probes. Then, signal intensity is determined for each cell by using a scanning confocal microscope. When a target nucleic acid binds to both probes, the signal intensity from the pooled probe region is stronger than the added signals of other two probe regions, as mentioned above.

The Examiner will note that while both the present invention and Gentalen use detection and comparison to determine the presence or absence of gene variations, there is a clear difference between the present invention and Gentalen in terms of what is being detected and what is being compared. Gentalen compares the signal detected as a result of the hybridization of the target sequence to the probes in the pooled region with the signal obtained from regions, which contain individual types of probes. To the contrary, in the present invention, a histogram of the total signal resulting from hybridization of the target sequence is compared with another histogram of the total signal obtained using a wild type sample. There are no "pooled" regions in the presently claimed invention, which are required in Gentalen.

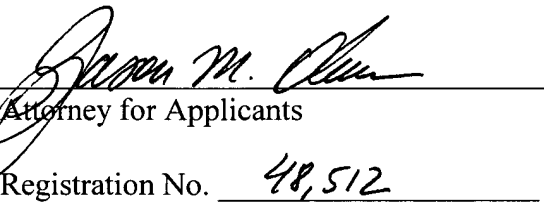
Thus, it is clear that Gentalen does not disclose or suggest determining signal intensity of groups of probe spots as presently claimed in order to obtain an intensity (histogram) pattern to be used to determine the presence or absence of a certain sequence. Accordingly, it is clear that Gentalen cannot affect the patentability of the presently claimed invention.

Applicants respectfully submit that new claims 24-28 are patentable over Gentalen for at least the reasons discussed above.

Wherefore, Applicants respectfully request that the outstanding rejection be withdrawn and that the present case be passed to issue.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our address given below.

Respectfully submitted,



Attorney for Applicants

Registration No. 48,512

FITZPATRICK, CELLA, HARPER & SCINTO
30 Rockefeller Plaza
New York, New York 10112-3801
Facsimile: (212) 218-2200

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